LISTING OF THE CLAIMS:

Applicants elect Group I, claims 1-10 and 13-16, with traverse and amend the claims as follows. This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method of identifying a protease which cleaves a substrate sequence, the method comprising the steps of:

(a) producing a library of mutein protease sequences, each different mutein protease sequence in the library being a member of the library, each member having ~~a protease scaffold with~~ N mutations relative to a wild-type scaffold sequence, wherein N is a positive integer,

(b) measuring the activity of ~~each member~~ at least two members of the library in cleaving the substrate sequence, and

(c) ~~comparing the activity of each member to the average activity of the library, thereby~~ identifying ~~which proteases have the highest~~ at least one mutein protease having an increased cleavage activity, ~~wherein N is a positive integer~~ relative to the wild-type scaffold sequence.

2. (Original) The method of claim 1, wherein the protease is a serine or cysteine protease.

3. (Currently amended) The method of claim 1, wherein N is an integer between 1 and 20.

4. (Currently amended) The method of claim ~~1~~ 3, wherein N is an integer from 1-5.

5. (Currently amended) The method of claim ~~1~~ 3, wherein N is an integer from 5-10.

6. (Currently amended) The method of claim ~~1~~ 3, wherein N is an integer from 10-20.

7. (Original) The method of claim 1, wherein the protease scaffold has the amino acid sequence of one of the members of the group consisting of trypsin, chymotrypsin, substilisin, thrombin, plasmin, Factor Xa, uPA, tPA, MTSP-1, granzyme A, granzyme B, granzyme M, elastase, chymase, papain, neutrophil elastase, plasma kallikrein, urokinase type plasminogen activator, complement factor serine proteases, ADAMTS13, neural endopeptidase/neprilysin, furin, and cruzain.

8. (Currently amended) The method of claim 1, wherein the substrate sequence is a sequence in a target protein that is involved with a pathology.

9. (Original) The method of claim 8, wherein the pathology is a member of the group consisting of rheumatoid arthritis, sepsis, cancer, acquired immunodeficiency syndrome, respiratory tract infections, influenza, cardiovascular disease, and asthma.

10. (Original) The method of claim 8, wherein the target protein is involved in a way that it causes the pathology.

11. (Withdrawn) The method of claim 1, wherein the target protein is involved in apoptosis.

12. (Withdrawn) The method of claim 11, wherein the target protein is caspase-3.

13. (Currently amended) The method of claim 1, wherein the activity of the detected protease is increased by at least 10-fold compared to the ~~average~~ activity of the ~~library~~ wild-type scaffold sequence.

14. (Currently amended) The method of claim 1, wherein the activity of the detected protease is increased by at least 100-fold compared to the ~~average~~ activity of the ~~library~~ wild-type scaffold sequence.

15. (Currently amended) The method of claim 1, wherein the activity of the detected protease is increased by at least 1000-fold compared to the ~~average~~ activity of the ~~library~~ wild-type scaffold sequence.

16. (Currently amended) The method of claim 1, further comprising the steps of:

(d) providing two or more members of the protease library identified with increased cleavage activity,

(e) combining the mutations on a first scaffold with the mutations on a second scaffold to produce a third scaffold; and

(f) identifying whether the combination produces a combined specificity protease that has increased cleavage activity in regards to the substrate sequence.

17-44. (Canceled)

45. (New) The method of claim 1, wherein the steps are repeated iteratively to create a variant protease comprising the desired specificity and selectivity.

46. (New) The method of claim 45, further comprising comparing the activity of the identified mutein protease against a mutein protease identified in an earlier iteration of the method, and identifying the mutein protease having increased activity.

47. (New) The method of claim 1, further comprising comparing the activity of the identified mutein protease against its corresponding wild type protease.

48. (New) The method of claim 1, wherein the substrate sequence is a sequence in a human protein.

49. (New) The method of claim 8, whereby cleaving the substrate sequence modifies the substrate, thereby having a therapeutic effect on the pathology.

50. (New) The method of claim 1, further comprising the steps of providing at least one mutein protease identified in step (c), and testing the mutein protease in a cell-based assay against a target protein comprising the substrate sequence.

51. (New) The method of claim 50, wherein the member of the library identified in step (d) has the highest measured cleavage activity.

52. (New) The method of claim 50, wherein the cell-based assay is an *in vivo* assay.

53. (New) A method of identifying a protease which cleaves a substrate sequence, the method comprising the steps of:

(a) producing a library of mutein protease sequences, each different mutein protease sequence in the library being a member of the library, each member having N mutations relative to a wild-type scaffold sequence, wherein N is a positive integer;

(b) measuring the activity of at least two members of the library in cleaving the substrate sequence;

(c) identifying at least one mutein protease having a measured increase in cleavage activity relative to the wild type scaffold sequence;

(d) providing two or more members of the protease library identified with increased cleavage activity;

(e) combining the mutations on a first scaffold with the mutations on a second scaffold to produce a third scaffold;

(f) identifying whether the combination produces a combined specificity protease that has increased cleavage activity toward the substrate sequence; and

(g) comparing the activity of the test mutein against the wild type scaffold, or some other reference sequence, or to an earlier version identified during an iterative process of incrementally selecting for increasing activity.

54. (New) The method of claim 53, the method further comprising the steps of:

(h) providing at least one mutein protease identified in step (c); and

(i) testing the mutein protease in a cell-based assay against a target protein comprising the substrate sequence.

55. (New) The method of claim 54, whereby cleaving the substrate sequence modifies the substrate, thereby having a therapeutic effect on the pathology.

56. (New) The method of claim 53, wherein the cell-based assay is an *in vivo* assay.

57. (New) The method of claim 53, wherein the steps are repeated iteratively to create a variant protease comprising the desired specificity and selectivity.

58. (New) The method of claim 53, wherein the substrate sequence is a sequence in a human protein.